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Preliminary Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

5 **Listing of the Claims**

Claim 1 (original): A method of treating a neurological disorder associated with synaptic vesicle function, endocrinopathy or hormonal diseases, comprising administering a compound or agent that modulates a function or activity of an SV2 protein.

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Claim 2 (original): A method of claim 1, wherein the neurological disorder is selected from the group consisting of seizure, epilepsy, Parkinson's disease, Parkinson's dyskinesias, migraine, Alzheimer's disease, neuropathic pain, essential tremor, cognitive disorders, and movement disorders.

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Claim 3 (original): A method of claim 1, wherein the compound or agent binds to the levetiracetam binding site of an SV2 protein.

20 Claim 4 (original): A method of modulating at least one function or activity of a SV2 protein in a cell, comprising exposing the cell to a compound or agent that binds to the levetiracetam binding site of the SV2 protein.

Claim 5 (original): A method of claim 4, wherein the compound or agent modulates the binding of levetiracetam to the levetiracetam binding site.

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Claim 6 (original): A method of discovering or modeling an interaction between an SV2 protein and a compound or agent selected from the group consisting of : levetiracetam, an analog or derivative of levetiracetam, or a compound or agent which competes with levetiracetam or an analog or derivative thereof for binding to the levetiracetam binding site comprising:

a) contacting the SV2 protein with the compound or agent; and
b) measuring and analyzing the interaction of the SV2 protein with the compound or agent.

5 Claim 7 (original): A method of claim 6 where the analysis is by proteolytic treatment of the SV2 proteins to observe a differential effect of binding of a ligand on proteolytic degradation.

Claim 8 (original): A method of claim 6, wherein the analysis is by 3-dimensional modeling or other purely computational techniques.

10 Claim 9 (original): A method of claim 8, wherein the 3-dimensional modeling is via nuclear magnetic resonance spectroscopy or X-ray crystallography.

Claim 10 (original): A method of claim 6, wherein the analysis is by binding studies.

15 Claim 11 (currently amended): A method of ~~any one of claims 6 or 10~~, wherein the SV2 protein is purified from natural sources.

20 Claim 12 (original): A method of claim 11 where the SV2 protein is purified from heterologously expressed protein driven from cloned nucleotide inserted in an expression vector, in a eukaryotic or prokaryotic host.

Claim 13 (original): A method of identifying a levetiracetam binding site within an SV2 protein comprising:

25 a) contacting a SV2 protein or fragment thereof with a compound or agent selected from the group consisting of levetiracetam, an analog or derivative of levetiracetam, or a compound or agent which competes with levetiracetam or an analog or derivative thereof for binding to the levetiracetam binding site; and

b) determining the binding of the compound or agent with the SV2 protein or fragment thereof.

5 Claim 14 (original): A method of claim 13, wherein the SV2 protein or fragment thereof comprises at least one amino acid substitution, deletion or addition.

10 Claim 15 (original): A method of claim 14, wherein the addition, deletion or substitution of amino acid residues removes at least one glycosylation sites.

15 Claim 16 (original): A method of claim 15, wherein the removal of glycosylation sites is via site-directed mutagenesis.

17 Claim 17 (original): A method of claim 13, wherein the SV2 protein is a fusion protein comprising at least one SV2 protein or fragment thereof and a fusion partner.

18 Claim 18 (original): A method of claim 17, wherein the fusion partner is a fusion tag.

20 Claim 19 (original): A method of claim 18, wherein the fusion tag is a poly-His tag or glutathione-S- transferase.

25 Claim 20 (original): A method of assaying the interaction between SV2 protein and a second protein comprising:

- a) expressing SV2 protein and the protein of interest in a cell;
- b) exposing the cell to a compound or agent which binds to the levetiracetam binding site; and
- c) determining the interaction between the SV2 protein and the protein of interest.

Claim 21 (original): A method of claim 20, wherein the second protein is selected from the group consisting of : a cell membrane protein, a vesicle membrane protein, a cytoplasmic

protein, a cytoskeletal protein, and an intracellular matrix protein.

Claim 22 (original): A method of claim 20, wherein the protein of interest is synaptotagmin.

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Claim 23 (original): A method of claim 20, wherein the protein of interest is a member of the SNARE complex.

10 Claim 24 (original): A method of claim 23, wherein the member of the SNARE complex is synaptic vesicle associated VAMP/synaptobrevin, syntaxin, or SNAP-25.

Claim 25 (original): A method of claim 20, wherein the SV2 protein lacks at least one glycosylation site.

15 Claim 26 (original): A method of identifying a compound or agent that modulates a neurological disorder associated with synaptic function, endocrinopathy or hormonal disease comprising:

- a) exposing a SV2 protein to the compound or agent; and
- b) determining whether the compound or agent modulates an activity of the SV2 protein.

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Claim 27 (currently amended): A method of ~~any one of~~ claim 3, 4, 5, 6, 20, or 26, wherein the compound or agent is levetiracetam or an analog or derivative thereof, or an anti-SV2 antibody or fragment thereof.

25 Claim 28 (currently amended): A method of ~~any one of~~ claims 13 or 27, wherein the compound or agent competes with levetiracetam or an analog or derivative thereof for binding to the levetiracetam binding site.

Claim 29 (currently amended): A method of ~~any one of~~ claims 13 or 27, wherein the

compound or agent is an antiSV2 antibody or fragment thereof.

Claim 30 (original): A method of claim 29, wherein the anti-SV2 antibody or fragment thereof binds to the levetiracetam binding site of SV2 protein.

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Claim 31 (original): A method of claim 29, wherein the anti-SV2 antibody or fragment thereof is selected from the group consisting of a polyclonal antibody and a monoclonal antibody.

10 Claim 32 (original): A method of claim 31, wherein the antibody fragment is selected from the group consisting of an Fab fragment, Fab'fragment, F (ab')2 fragment and anscFv fragment.

15 Claim 33 (original): A method of claim 31, wherein the monoclonal antibody is selected from the group consisting of a chimeric antibody, a humanized antibody, and a human antibody.

20 Claim 34 (original): A method of identifying a cellular response to a compound or agent selected from the group consisting of levetiracetam, an analog or derivative of levetiracetam, or a compound or agent which competes with levetiracetam or an analog or derivative thereof for binding to the levetiracetam binding site comprising:

- a) exposing cells expressing an SV2 protein to the compound or agent; and
- b) analyzing a change in the expression of a nucleic acid or protein in the exposed cell.

25 Claim 35 (currently amended): A method of ~~any one of~~ claims 20 or 34, wherein the step of exposing the cell to a compound or agent which binds to the levetiracetam binding site is carried out under conditions with a divalent cation concentration selected from the group consisting of less than about 1pM, between about 1 uM and about 1000pM, and at least about 1000uM.

Claim 36 (original): An isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO:5 or the complement thereof.

5 Claim 37 (currently amended): An isolated polypeptide comprising an amino acid sequence encoded by the isolated nucleic acid molecule of claim 12336.

Claim 38 (currently amended): An isolated polypeptide of claim 124 37, comprising the amino acid sequence of SEQ ID NO : 6.

10 Claim 39 (original): A method of claim 26, wherein the step of determining whether the compound or agent modulates an activity of the SV2 protein is selected from the group consisting of

- a) measuring transport of at least one monovalent cation or divalent cation across a membrane;
- 15 b) measuring SNARE complex formation;
- c) measuring Ca²⁺ channel formation or activity;
- d) measuring SV2 interaction with at least one other protein;
- e) measuring transport of at least one substrate across a membrane; and,
- f) measuring synaptic vesicle fusion, exocytosis, or synaptic vesicle recycling.

20 Claim 40 (original): A method of claim 39, wherein the monovalent cation is selected from the group consisting of H⁺, Cl⁻, Na⁺ and K⁺.

25 Claim 41 (currently amended): A method of ~~any one of~~ claim 35 or 39, wherein the divalent cation is selected from the group consisting of Ca²⁺, Zn²⁺ Pb²⁺ Mg²⁺ Mn²⁺ F²⁺ d C²⁺.

Claim 42 (currently amended): A method of claim 41, wherein the at least one divalent cation is Ca₂₊

Claim 43 (original) A method of claim 39, wherein the at least one other protein is synaptotagmin.

5 Claim 44 (original): A method of claim 39, wherein the at least one other protein is laminin-1.

10 Claim 45 (original): A method of claim 39 wherein the at least one substrate is selected from the group consisting of amines, acetylcholine, excitatory neurotransmitters, GABA, serotonin, glycine or other amino acids, sugars and organic ions.

Claim 46 (original): A method of identifying a binding partner for a SV2 protein, comprising:

- a) exposing a SV2 protein or fragment to a potential binding partner;
- 15 b) incubating the protein or fragment and potential binding partner with (2S)-2-[4- (3-azidophenyl)-2-oxopyrrolidin-1-yl] butanamide; and
- c) determining if the binding of(2S)-2- [4- (3-azidophenyl)-2-oxopyrrolidin-1- yl] butanamide to the protein is inhibited by the potential binding partner, thereby identifying binding partner for the protein.

20 Claim 47 (original): A method of identifying a compound or agent useful for the treatment of a neurological or endocrinological disorder, comprising:

- a) exposing a SV2 protein or fragment to the agent and levetiracetam or an analog or derivative thereof; and
- 25 b) determining if the binding of levetiracetam or an analog or derivative thereof to the protein is modulated by the agent, thereby identifying an agent useful for the treatment of a neurological disorder.

Claim 48 (original): A method of claim 47, wherein the levetiracetam or an analog or

derivative thereof is directly or indirectly labeled.

Claim 49 (original): A method of claim 47, wherein the SV2 protein or fragment is incubated with the levetiracetam or an analog or derivative prior to the agent, after addition of 5 the agent, or concurrent with the agent.

Claim 50 (original): A method of claim 47, wherein the SV2 protein or fragment is incubated with levetiracetam.

10 Claim 51 (original): A method of claim 47, wherein the neurological disorder is selected from the group consisting of epilepsy; epileptogenesis; seizure disorders; convulsions; withdrawal seizures; neurological disorders; bipolar disorders; mania; depression; anxiety; migraine; neuralgia; trigeminal neuralgia; chronic pain conditions; neuropathic pain; anaesthesia-related hyperexcitability; cerebral ischemia; head trauma; myotonia; excitatory states provoked by 15 drug or alcohol abuse, dependence or withdrawal; stroke; myoclonus; essential tremor; tics; Tourette's syndrome; dyskinesia; spasticity; movement disorders; neonatal cerebral haemorrhage; amyotrophic lateral sclerosis; Parkinson's disease; Alzheimer's disease; a neurodegenerative disease; and dementia.

20 Claim 52 (currently amended): A pharmaceutical composition comprising a compound or agent as identified in the method of ~~any one of claims 26 or 47~~ said compound being different from ~~a compound as described in Fig. 15~~ levetiracetam or ucb 30889.

25 Claim 53 (currently amended): A method of treating a neurological or endocrinological disorder which comprises administering to an individual in need of such treatment a compound or agent as identified in the method of ~~any one of claims 26 or 47~~ said compound being different from ~~a compound as described in Fig. 15~~ levetiracetam or ucb 30889.

Claim 54 (original): A method according to claim 53, wherein the neurological disorder

is selected from the group consisting of epilepsy; epileptogenesis ; seizure disorders; convulsions; withdrawal seizures; neurological disorders; bipolar disorders; mania; depression; anxiety; migraine; neuralgia; trigeminal neuralgia; chronic pain conditions; neuropathic pain; anaesthesia-related hyperexcitability; cerebral ischemia; head trauma; myotonia; excitatory states 5 provoked by drug or alcohol abuse, dependence or withdrawal; stroke; myoclonus; essential tremor; tics; Tourette's syndrome; dyskinesia; spasticity; movement disorders; neonatal cerebral haemorrhage; amyotrophic lateral sclerosis; Parkinson's disease; Alzheimer's disease; a neurodegenerative disease; and dementia.

10 Claim 55 (original): A method according to claim 53 wherein the endocrinological disorders is selected from the group consisting of endocrinopathies involving hypersecretion or hyposecretion of at least one hormone; gigantism; dwarfism; adrenal-medulla-related diseases; hypoglycemia; and circulation shock.

15 Claim 56 (currently amended): A method of ~~any one of claims 1, 20, 26, 34, or~~ 47, wherein the SV2 protein is SV2A.

Claim 57 (original): A method of claim 56, wherein the SV2A protein comprises SEQ ID NO: 2.

20 Claim 58 (currently amended): A method of claim ~~any one of claims 13, 27, or~~ 47, wherein the analog or derivative of levetiracetam is(2S)-2- [4- (3-azidophenyl)-2-oxopyrrolidin-1-yl] butanamide.

25 Claim 59 (original): A method of claim 58, wherein the analog or derivative of levetiracetam is selected from the group consisting of N-alkylated 2-oxo-pyrrolidine derivatives, N-alkylated 2-oxopiperidinyl derivatives, and N-alkylated 2-oxo-azepanyl derivatives.

Claim 60 (original): A method of identifying an agent useful for the treatment of a neurological or endocrinological disorder, comprising:

a) exposing a SV2 protein or fragment to the agent;

b) incubating the protein or fragment and agent with(2S)-2- [4- (3-azidophenyl)- 2-

5 oxopyrrolidin-1-yl] butanamide ; and

c) determining if the binding of(2S)-2- [4- (3-azidophenyl)-2-oxopyrrolidin-1- yl]

butanamide to the protein is inhibited by the agent, thereby identifying binding partners for the protein.

10 Claim 61 (original): A method of discovering or modeling an interaction between an SV2 protein, or fragment or derivative thereof, and a compound or agent selected from the group consisting of : levetiracetam, an analog or derivative of levetiracetam, or a compound or agent which competes with levetiracetam or an analog or derivative thereof for binding to the levetiracetam binding site comprising:

15 a) creating a 3-dimensional model of the SV2 protein, or fragments thereof, via either biochemical, biophysical, purely computational techniques, or some combination of these; and

b) creating 3-dimensional model of one or a collection of potential ligands that might potentially bind the SV2 protein.

20 Claim 62 (original): A method of claim 61, further comprising using purely computational techniques to dock the 3-dimensional model of SV2 proteins with the 3-dimensional models of potential ligands.

25 Claim 63 (original): A method of discovering or modeling an interaction between an SV2 protein and a compound or agent selected from the group consisting of: levetiracetam, an analog or derivative of levetiracetam, or a compound or agent which competes with levetiracetam or an analog or derivative thereof for binding to the levetiracetam binding site comprising:

- a) determining a biochemical, pharmacological, organismal, cellular or molecular effect of a potential CNS active molecule in a genetically wild-type animal or in molecules, cells or tissues derived from such animals; and
- b) comparing the measured effect of that compound in an equivalent study in a system with an SV2 protein knocked out or knocked down.

5 Claim 64 (original): A method of isolating a functionally active membrane associated SV2 protein complex comprising: a) solubilizing tissues comprising the SV2 protein with a detergent; and b) isolating the SV2 protein complex.

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 Claim 65 (original): A method of claim 64, wherein the method further comprises purifying the SV2 protein complex by immunoaffinity.

15 Claim 66 (original): A method of claim 65, wherein the SV2 protein complex is further purified to obtain the SV2 protein.

 Claim 67 (original): A method of claim 64, wherein the detergent is n-dodecyl- -D-maltoside or derivatives or analogs thereof.

20 Claim 68 (original): A method of claim 64, wherein the tissues are brain membranes.

 Claim 69 (original): A method of claim 64, further comprising identifying the molecule or molecules complexed to the SV2 protein.

25 Claim 70 (currently amended): A method of ~~any one of claims~~ claim 64 to 69, wherein the SV2 protein is SV2A protein, SV2B protein, or SV2C protein.

 Claim 71 (original): A purified SV2 protein complex obtained by the method of claim 64.

Claim 72 (original): A purified SV2 protein complex of claim 71, wherein the SV2 protein is SV2A protein, SV2B protein, or SV2C protein.